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This newsletter is quarterly and contains abstracts from medical journals published between June and September 2008. Abstracts presented at scientific meetings may also be included. Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia

Vulvodynia incidence and remission rates among adult women: a 2-year follow-up study.

Reed BD, Haefner HK, Sen A, Gorenflo DW
Obstet Gynecol. 2008 Aug;112(2 Pt 1):231-7.

OBJECTIVE: To estimate the incidence and remission rates of vulvodynia over a 2-year period.
METHODS: A 2-year follow-up survey was sent to the University of Michigan Women's Health Registry members who had participated in a previously reported, validated survey. Changes in clinical status, incidence, and remission rates for vulvodynia were estimated, as were factors associated with new onset or remission of symptoms, using univariable and multivariable analyses. **RESULTS:** Of 1,037 women enrolled in the initial study, 744 women (71.7%) completed an online or written follow-up survey between September 2006 and March 2007. Of the 372 asymptomatic women controls at initial enrollment, 13 (3.5%, 95% confidence interval 1.6-5.4%) had developed vulvodynia during the 2-year follow-up period; nine (2.2%) of these had ongoing symptoms. Of 45 women with vulvodynia at initial enrollment, 10 (22.2%, 95% confidence interval 10.1-34.4%) indicated their symptoms had resolved. Factors at enrollment that were associated with incidence of vulvodynia were younger age and history of pain after intercourse. Remission was more common in women who did not have pain after intercourse and in those who reported less severe pain at enrollment. **CONCLUSION:** Based on 2-year follow-up, each year approximately one in 50 women develop symptoms of vulvodynia, and one in 10 women with vulvodynia report remission of symptoms.

A search for *helicobacter pylori* in localized vulvodynia.

Geva A, Sabo E, Levy J, Blumenthal M, Ophir E, Geva H, Bornstein J
Gynecol Obstet Invest. 2008 Jun 6;66(3):152-156.

Background: We noted that several patients presenting with both localized vulvodynia (vulvar vestibulitis) and peptic symptoms reported a resolution of dyspareunia after receiving a full treatment course for *Helicobacter pylori*. **Methods:** Women with localized vulvodynia were interviewed regarding symptoms of peptic disease. Those with peptic symptoms underwent a blood test for the presence of antibodies to *H. pylori* and were referred to a gastroenterology consultation. In all women, vestibular biopsies were obtained and stained for *H. pylori*. Healthy vestibular tissues as well as archival negative and positive gastric tissues served as controls. **Results:** Of the blood antibody tests, 12 (80%) were positive. None of the patients had evidence of *H. pylori* in the vestibule. Eleven women received triple therapy for eradication of *H. pylori*. Eight (73%) reported complete relief of dyspareunia and of gastric symptoms.

Conclusion: Our study found no immunohistochemical evidence of *H. pylori* infection in the vestibule but suggested a possible role for anti-*H. pylori* treatment in localized vulvodynia.

Umbilical hypersensitivity in women with primary vestibulodynia.

Burrows LJ, Klingman D, Pukall CF, Goldstein AT
J Reprod Med. 2008 Jun;53(6):413-6.

OBJECTIVE: To provide evidence that primary vestibulodynia (PV) is a congenital defect in tissue derived from the primitive urogenital sinus. STUDY DESIGN: Twenty-two women with PV, 16 with secondary vestibulodynia (SV) and 8 controls were included in this study. Subjects underwent a complete history and physical examination, including assessment with a vulvalgesiometer to measure the sensory and pain detection thresholds in the vulvar vestibule, deltoid and umbilicus. RESULTS: The median vestibular sensitivity was 5 g in the PV group and 10 g in the SV group ($p = 0.77$). The median umbilical pain thresholds for the PV, SV and control groups were 115, 675 and 500 g, respectively. Women with PV displayed a significantly higher level of umbilical sensitivity (a substantially lower pain threshold) compared with women with SV and the control group ($p = 0.0001$ and 0.002 , respectively). There was no difference in umbilical sensitivity between the SV and control groups. CONCLUSION: Because both the umbilicus and vulvar vestibule are derived from primitive urogenital sinus, this suggests that women with PV may have a congenital abnormality in urogenital - sinus-derived epithelium.

McGill pain questionnaire findings among women with vulvodynia and chronic yeast infection.

Saunders NA, Reed BD, Haefner HK
J Reprod Med. 2008 Jun;53(6):385-9.

OBJECTIVE: To determine whether patients referred for vulvar pain or candidiasis had different characteristics of pain as measured by the McGill Pain Scale or the number of McGill categories chosen. STUDY DESIGN: Data were collected at the University of Michigan Center for Vulvar Diseases between April 1998 and March 2003. The association between the McGill pain score and the number of McGill categories selected with the diagnostic categories of vestibulodynia, generalized vulvodynia and chronic yeast infections were evaluated. RESULTS: A total of 196 women presented with vulvodynia (105 women with vestibulodynia, 91 women with generalized vulvodynia) and 50 women presented with *Candida* vulvovaginitis. The vulvodynia groups had McGill scores and numbers of categories selected that were increased compared with the *Candida* group (24.16 ± 13.03 and 24.37 ± 12.82 vs. 16.20 ± 10.21 for the McGill score, $p < 0.001$, and 9.22 ± 4.11 and 9.87 ± 4.44 vs. 7.30 ± 3.70 for the numbers of categories selected, $p = 0.002$). CONCLUSION: Patients presenting with complaints of a yeast infection have a statistically lower McGill pain score and McGill pain indicators compared with patients with vulvar pain.

Vulvodynia: A review of pathophysiological factors and treatment options.

Pukall CF, Bergeron S, Goldfinger C
Basic & Clinical Medicine. April 2008;28(4):421-36.

Vulvodynia, or chronic vulvar pain, affects 16% of US women in the general population and has negative effects on numerous aspects of a woman's life. The purpose of this paper is to review the literature on the etiology and treatment of vulvodynia. Since relatively little research has been carried out on unprovoked generalized vulvodynia (UGVD), this review focuses on provoked vestibulodynia (PVD), a subtype of vulvodynia characterized by a severe, burning/sharp pain that occurs in response to pressure localized to the vestibule. Research examining the pathophysiology of PVD provides evidence that both peripheral (e.g., vestibular tissue abnormalities, pelvic floor hypertonicity) and central (e.g., increased neural activation) factors are involved in the development and maintenance of PVD. Additionally, psychological reactions to the pain may vary and influence the expression and course of the pain. Despite the multitude of factors involved in PVD, most treatment studies to date are unimodal in nature, retrospective, and uncontrolled. A review of treatment strategies targeting peripheral (e.g., topical applications, vestibulectomy) and central (e.g., antidepressants, pain management therapy) components

of PVD is provided, and the need for multimodal treatment plans which target both levels of pain processing is discussed. Given the complexity of PVD, a biopsychosocial is recommended for future research endeavors and treatment plans.

Sites of pain from interstitial cystitis/painful bladder syndrome.

Warren JW, Langenberg P, Greenberg P, Diggs C, Jacobs S, Wessellmann U
J Urol. 2008 Aug 14. [Epub ahead of print]

PURPOSE: In interstitial cystitis/painful bladder syndrome multiple pain sites are common. We hypothesized that a careful and systematic description of the pain of interstitial cystitis/painful bladder syndrome might provide clues to its pathogenesis. **MATERIALS AND METHODS:** Women with 12 months or greater of interstitial cystitis/painful bladder syndrome symptoms underwent a medical record review and interview. Each completed a questionnaire that included views of the female body and described up to 5 interstitial cystitis/painful bladder syndrome pains, noting 40 descriptors for each. **RESULTS:** Two-thirds of the 226 patients reported multiple pains. Pain could be consolidated at 4 sites, including suprapubic, urethral, genital and nongenitourinary. Most descriptors were similar and little evidence indicated that 1 pain influenced pain at another site. Another 3 patterns were evident, including 1) a suprapubic > urethral > genital > nongenitourinary ranking in site distribution and at each site proportions that were solitary, the worst and the most frequent pains, and pains that responded to bladder events, 2) site specific allodynia, and 3) for urethral and genital pains a wider spectrum of sensations, including burning, stinging and sharp. Patients with urethral (38%) or genital (27%) pain did not differ from those without such pain in 95% of 44 important characteristics. **CONCLUSIONS:** Suprapubic prominence and changes in the voiding cycle are features consistent with but do not prove that the bladder is the pain generator in interstitial cystitis/painful bladder syndrome and the pain sites described by patients are referred from it. The patients with interstitial cystitis/painful bladder syndrome who might have been diagnosed with vulvodynia or urethral syndrome did not differ from others in important patient variables.

Post-coital burning pain and pain at micturition: early symptoms of partial vaginismus with or without vulvar vestibulitis?

Engman M, Wijma K, Wijma B
J Sex Marital Ther. 2008;34(5):413-28

Twenty-four women with partial vaginismus with or without vulvar vestibulitis participated in a semi-structured telephone interview concerning early signs and development of their pain symptoms during/after intercourse. At the onset of the problem, pain after intercourse was more common than pain during penetration. Pain intensity during penetration increased from the onset of the problem to when the women ceased having intercourse. Pain during penetration lasted for 1 minute, and was most often described as sharp/incisive/bursting, while pain after intercourse had a duration of 2 hours and was described as burning and/or smarting. Post-coital pain during micturition was described by 70% of the women.

Genital restlessness (vulvodynia) events accompanying restless legs syndrome.

Akcali A, Ferini-Strambi L, Kaynak H, Karadeniz D, Akcali C
Sleep Med. 2008 Jun 24. [Epub ahead of print]

No abstract available.

Topical gabapentin in the treatment of localized and generalized vulvodynia.

Boardman LA, Cooper AS, Blais LR, Raker CA
Obstet Gynecol. 2008 Sep;112(3):579-85.

OBJECTIVE: To evaluate the clinical efficacy and tolerability of topical gabapentin in the treatment of women with vulvodynia. **METHODS:** A retrospective study was designed to ascertain clinical responses to topical gabapentin. Patient demographic and medical characteristics, including present and prior treatment for vulvodynia, were routinely collected. The final outcome was defined by a comparison between pretreatment and posttreatment mean pain scores based on a discrete visual analog scale of 0 to 10. Categorical data were compared by Fisher exact test, continuous variables between groups by the Wilcoxon rank sum test, and mean change in pain score between pretreatment and posttreatment by paired Student t test. **RESULTS:** Between January 2001 and December 2006, 51 women with vulvodynia (19 or 37% with generalized vulvodynia, 32 or 63% with localized) were treated with 2% to 6% gabapentin. After a minimum of 8 weeks of therapy, the mean pain score among the 35 evaluable women was significantly reduced from 7.26 to 2.49 (mean change -4.77, 95% confidence interval -5.47 to -4.07). Overall, 28 of 35 (80%) demonstrated at least a 50% improvement in pain scores. Among patients with localized vulvodynia, sexual function improved in 17 of 20 with evaluable results (6 of 9 reinstated vaginal intercourse, whereas all 11 patients experiencing decreased frequency of intercourse reported increased frequency after treatment). Discontinuations occurred in 7 of 50 (14%) treated. **CONCLUSION:** Topical gabapentin seems to be well-tolerated and associated with significant pain relief in women with vulvodynia. **LEVEL OF EVIDENCE:** III.

Is modified vestibulectomy for localized provoked vulvodynia an effective long-term treatment? A follow-up study.

Eva LJ, Narain S, Orakwue CO, Luesley DM
J Reprod Med. 2008 Jun;53(6):435-40.

OBJECTIVE: To determine whether vestibulectomy is an effective long-term treatment and investigate the levels of patient satisfaction in women with localized provoked vulvodynia, and to provide long-term follow-up data from a cohort of women whose short-term success rates have been published previously. **STUDY DESIGN:** A retrospective case note review of 110 women with localized provoked vulvodynia and follow-up patient questionnaire. Patients were asked to quantify their pain scores before surgery, at 2 months after surgery and 1 year after surgery and score their satisfaction levels. **RESULTS:** Mean pain scores continued to improve throughout the first postoperative year. The mean score was 9.17 preoperatively, 5.24 at 2 months after surgery and 2.48 at 1 year after surgery. Eighty-three percent of patients would recommend the procedure as effective treatment of localized provoked vulvodynia. The overall mean satisfaction score was 7.96, and long-term success appears to be reflected by short-term results. **CONCLUSION:** Vestibulectomy is an effective long-term treatment for women with provoked localized vulvodynia; the procedure is associated with high levels of patient satisfaction and low complication rates. Short-term success appears to be a good indicator of long-term improvement, and improvement continues throughout the first postoperative year.

Patients' assessments of a superficial modified vestibulectomy for vestibulodynia.

Goetsch MF
J Reprod Med. 2008 Jun;53(6):407-12.

OBJECTIVE: To assess long-term outcomes of surgical treatment of vestibulodynia by reporting patients' tabulated questionnaire responses. **STUDY DESIGN:** Between 1988 and 2006, 133 subjects underwent modified superficial vestibulectomies. At 4 time intervals, portions of the expanding cohort were queried with a mailed questionnaire. Results were compared to the clinical findings. Questionnaires had closed questions, ranked and non-ranked, as well as open questions and visual analogue scales. Percentages were calculated by SPSS statistical software. **RESULTS:** A total of 119 women (89%) returned questionnaires, allowing a mean follow-up interval of 2.8 years; 68% reported that dyspareunia was cured completely, and for 24% it was lessened. Twenty-two percent said they perceived a different pain after

surgery, many identifying it as muscular. Eighty-seven percent said they would have the procedure again. Qualitative responses revealed the importance of physical therapy, the complexities of pain issues, the toll on emotions and relationships and suggestions for more education of health practitioners and women generally about this entity. **CONCLUSION:** A large majority of women who underwent superficial vestibule surgery for vestibulodynia found it quite acceptable and instrumental in treating dyspareunia. Many wished they had had it sooner. Individualized, superficial surgery is very effective and should not be withheld if short-term medical and physical therapy have proven to be incomplete therapies.

Transcutaneous electrical nerve stimulation to treat vestibulodynia: a randomized controlled trial.

Murina F, Bianco V, Radici G, Felice R, Di Martino M, Nicolini U
BJOG. 2008 Aug;115(9):1165-70.

OBJECTIVE: To assess the efficacy of transcutaneous electrical nerve stimulation (TENS) in the treatment of vestibulodynia. **DESIGN:** Double-arm randomised placebo-controlled trial. **SETTING:** An outpatient department for vulval disease. **POPULATION:** Forty women with vestibulodynia, a vestibular discomfort mostly reported as a burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurological disorder. **METHODS:** Twice a week active TENS or sham treatment were delivered through a vaginal probe via a calibrated dual channel YSY-EST device. Women of both groups underwent 20 treatment sessions. **MAIN OUTCOME MEASURES:** Visual analogue scale (VAS), the short form of the McGill-Melzack Pain Questionnaire (SF-MPQ), the Marinoff Scale for dyspareunia and the Female Sexual Function Index questionnaire (FSFI) were assessed at baseline, at the end of treatment and at follow up 3 months after the end of treatment. **RESULTS:** The VAS and SF-MPQ scores (6.2 +/- 1.9 and 19.5 +/- 11.9 before treatment, respectively) improved significantly in the active TENS group (2.1 +/- 2.7, P= 0.004 and 8.5 +/- 10.7, P= 0.001, respectively), but not in the placebo group. The Marinoff dyspareunia scale and the FSFI also showed a significant improvement. **CONCLUSIONS:** TENS is a simple, effective and safe short-term (3 months) treatment for the management of vestibulodynia.

Nitric oxide: New evidence for novel therapeutic indications.

Wimalawansa SJ
Expert Opin Pharmacother. 2008 Aug;9(11):1935-54.

BACKGROUND: Nitric oxide (NO) deficiency is implicated in many pathophysiological processes in mammals. NO is a ubiquitous molecule involved in multiple cellular functions. Uncontrolled or inappropriate production of NO may lead to several disease states including septic shock, rheumatoid and inflammatory arthropathies, and expansion of cerebral damage after stroke. However, to date, there are no therapeutic agents available that can overcome these conditions. Similarly, underproduction of NO by NO synthase or enhanced breakdown of NO also leads to diseases such as hypertension, ischemic conditions, pre-eclampsia, premature delivery, among others. NO donor therapies are indicated in these conditions. **RESULTS:** Nitroglycerin and nitrates (NO donors) have been used as therapeutic agents for the past century, particularly to treat vascular disease, and the only significant adverse effects are headaches. NO donors are highly cost-effective and have beneficial effects in multiple body systems. When the body cannot generate NO via NO synthase or due to rapid turnover leading to inadequate amounts of NO available for biological homeostasis, administration of exogenous NO, or prolongation of the actions of endogenous NO, are practical ways to supplement NO. **CONCLUSION:** Recipients of such therapy include patients with angina pectoris, coronary artery disease, hypertension, osteoporosis, gastrointestinal motility disorders, pregnancy-related disorders including premature delivery, pre-eclampsia, vulvodynia, and erectile dysfunction in men. Postmenopausal NO deficiency is rectified with hormone replacement therapy, which enhances local production of NO. Declining local NO production secondary to estrogen deficiency in postmenopausal women and perhaps in older men could be one of the reasons for age-related increased incidences of cardiovascular events and sexual dysfunction. Thus, in addition to supplementation of NO compounds in acute situations like alleviating angina and erectile dysfunction, chronic NO therapy is cost-effective in decreasing cardiovascular events, and improving the urogenital system and skeletal health.

Evidence for the use of botulinum toxin in the chronic pain setting – a review of the literature.

Jevnes LC, Gauci CA

Pain Pract. 2008 Jul-Aug;8(4):269-76.

A significant proportion of chronic pain is of musculoskeletal origin. Botulinum toxin (BTX) has been successfully used in the treatment of spasmodic torticollis, limb dystonia, and spasticity. Investigators have, thus, become interested in its potential use in treating many chronic pain conditions. Practitioners have used BTX, outside the product license, in the treatment of refractory myofascial pain syndrome and neck and low back pain (LBP). This article reviews the current evidence relating to chronic pain practice. There is evidence supporting the use of both BTX type A and type B in the treatment of cervical dystonias. The weight of evidence is in favor of BTX type A as a treatment in: pelvic pain, plantar fasciitis, temporomandibular joint dysfunction associated facial pain, chronic LBP, carpal tunnel syndrome, joint pain, and in complex regional pain syndrome and selected neuropathic pain syndromes. The weight of evidence is also in favor of BTX type A and type B in piriformis syndrome. There is conflicting evidence relating to the use of BTX in the treatment whiplash, myofascial pain, and myogenous jaw pain. It does appear that BTX is useful in selected patients, and its duration of action may exceed that of conventional treatments. This seems a promising treatment that must be further evaluated.

Painful perineum in all its forms. Contribution of manual medicine and osteopathy. Clinical study.

[article in French]

Grimaldi M

J Gynecol Obstet Biol Reprod (Paris). 2008 Sep;37(5):449-56.

No satisfactory therapy has yet been found to relieve many chronic pelviperineal pains such as Dyspareunia, Vulvodynia, Coccygodynia and others pelvic various pains, although these can be highly disruptive in everyday life. They may be brought on by an osteo-myo-fascial disorder, often undetected despite the possibility to effectively treat, this condition using manual medicine in the gynaecologist's office. A framed clinical examination protocol as well as a therapeutic one are offered in this novel approach still rarely implemented in gynaecology. Such treatment is documented in six typical clinical cases and a global study on 86 patients with disruptive chronic pelviperineal pain, showing 71% satisfactory results following two manual medicine sessions. These very encouraging results need to be confirmed on a larger scale in order to establish an appropriate teaching protocol.

Dyspareunia in postmenopausal women: A critical review.

Kao A, Binik YM, Kapuscinski A, Khalife S

Pain Res Manag. 2008 May-Jun;13(3):243-54.

BACKGROUND: Dyspareunia, or pain during sexual intercourse, is among the problems most frequently reported by postmenopausal women. Past literature has almost unanimously attributed dyspareunic pain occurring during or after the menopausal transition to declining estrogen levels and vaginal atrophy. **OBJECTIVES:** To critically review the literature on the prevalence, risk factors, etiology, clinical presentation and treatment of postmenopausal dyspareunia. The present review also examines the traditional and widely held conceptualization of postmenopausal dyspareunia as a direct symptom of hormonal decline. **METHODS:** Searches of medical and psychological databases were performed for relevant articles and empirical studies. The methodological quality and outcomes of the studies were systematically reviewed. **RESULTS:** Available empirical evidence suggests that dyspareunia is common in postmenopausal women, and that it is not highly correlated with menopausal status, estrogen levels or vaginal atrophy. Decreasing levels of endogenous estrogen contribute to the development of dyspareunia in postmenopausal women suffering from vaginal atrophy. Hormonal supplementation is beneficial in alleviating their pain. However, a substantial proportion of treated women do not report relief. **CONCLUSIONS:** Postmenopausal dyspareunia occurring concurrently with vaginal atrophy is strongly associated with a lack of estrogen in the genital tract. However, a significant percentage of postmenopausal women experience dyspareunic pain that is not caused by hypoestrogenism. It is likely that other types of dyspareunia that occur premenopausally are also occurring in postmenopausal

women. Research is needed to adequately address this issue. A change in perspective toward a multi-axial pain-focused approach is proposed for future research concerning dyspareunia in postmenopausal women.

Vulvodynia: Definition, diagnosis and treatment.

Damsted Petersen C, Lundvall L, Kristensen E, Giraldi A
Acta Obstet Gynecol Scand. 2008 Aug 13:1-9.

Vulvodynia is a chronic painful disorder with an estimated prevalence of 9-12%. A rising incidence of the condition constitutes a growing problem. This has led to an increased focus on etiology and treatment, while the definition also requires attention. Previous assumptions stating that the problem is solely a psychological disorder have been abandoned, because inflammatory mechanisms and genetic factors have been found to be involved in the pathogenesis as well as psychosexual contributors. This article describes the terminology and definition of the condition, theories on patho-physiological mechanisms underlying the disorder, methods of diagnosis and evidence and recommendations on clinical management. A critical examination of the literature regarding vulvodynia reveals numerous strategies and recommendations for treatment, many of which are not evidence-based, and a lack of effective treatment for all patients. Research is being undertaken internationally to find more specific and unequivocal causes of the disorder, as well as to develop evidence-based methods of treatment.

Determining the cause of vulvovaginal symptoms.

Farage MA, Miller KW, Ledger WJ
Obstet Gynecol Surv. 2008 Jul;63(7):445-64.

Both patients and clinicians may incorrectly diagnose vulvovaginitis symptoms. Patients often self-treat with over-the-counter antifungals or home remedies, although they are unable to distinguish among the possible causes of their symptoms. Telephone triage practices and time constraints on office visits may also hamper effective diagnosis. This review is a guide to distinguish potential causes of vulvovaginal symptoms. The first section describes both common and uncommon conditions associated with vulvovaginitis, including infectious vulvovaginitis, allergic contact dermatitis, systemic dermatoses, rare autoimmune diseases, and neuropathic vulvar pain syndromes. The focus is on the clinical presentation, specifically 1) the absence or presence and characteristics of vaginal discharge; 2) the nature of sensory symptoms (itch and/or pain, localized or generalized, provoked, intermittent, or chronic); and 3) the absence or presence of mucocutaneous changes, including the types of lesions observed and the affected tissue. Additionally, this review describes how such features of the clinical presentation can help identify various causes of vulvovaginitis.

Tarlov's cyst: Definition, etiopathogenesis, proaedeutic and treatment.

[Article in Portuguese]

De Sa MC, D'Angelo CT, Da Ros Malacarne G, Neto P, Pagura J
Acta Med Port. 2008 Mar-Apr;21(2):171-8. Epub 2008 Jul 26.

Tarlov's cyst or perineurial cyst is disease on portion of the posterior nerve root in lumbo-sacral region. The lack of knowledge of physicians around the world about Tarlov's cyst as to their nature, significance and treatment also with differential diagnostics to radiculopathy in legs. With review of literature discuss about definition, etiopathogenesis, diagnostic investigation and treatment clinic and/or surgery. The pathogenesis Tarlov's cyst remains unclear; several cases have history of the trauma, old hemorrhage, congenital and iatrogenic. Cysts provoke low back pain, sacral radiculopathy, dyspareunia, urinary incontinence. The magnetic resonance imaging is now the gold standard to diagnose cysts. The treatment is clinic or surgery depending neurologics finding and neuroimage.

Vulvar pain: A phenomenological study of couples in search of effective diagnosis and treatment.

Connor JJ, Robinson B, Wieling E
Fam Process. 2008 Jun;47(2):139-55.

Vulvar vestibulitis syndrome (VVS), a vulvar pain disorder, continues to puzzle medical and mental health professionals due to its unknown etiology and lack of effective treatment. This study used transcendental phenomenology methodology to explore the experiences of couples in which the woman has a diagnosis of VVS. Sixteen in-depth semi-structured interviews were conducted with 13 heterosexual couples and 3 women. Four essences emerged: (1) In search of ... the medical journey required extensive searching for knowledgeable and respectful practitioners to provide treatment. (2) The process of developing a personal understanding of this disorder led many couples to question their role in causing and maintaining VVS. (3) Developing strategies for coping with painful intercourse led to three strategies: becoming non-sexual, using alternatives to vaginal sex, and altering or enduring painful intercourse. (4) Feelings of isolation were experienced as adapting to this chronic pain syndrome was often a lonely process. Clinical suggestions included: treating the couple, not just the woman with VVS; encouraging couples to broaden definitions about the importance and primacy of vaginal intercourse and suggest alternative sexual activities less likely to cause vulvar pain; developing shared meaning as a couple, and assisting couples in locating physicians and resources. Suggestions are relevant for couples with VVS and those with chronic health problems affecting sexual relationships.

Male partners of women with provoked vestibulodynia: Attributions for pain and their implications for dyadic adjustment, sexual satisfaction, and psychological distress.

Jodoin M, Bergeron S, Khalife S, Dupuis MJ, Desrochers G, Leclerc B
J Sex Med. 2008 Jul 15. [Epub ahead of print]

Introduction. Provoked vestibulodynia is a female genital pain condition that results in sexual dysfunction and impacts negatively on the couple. Although patients' causal attributions have been linked to worse psychosexual outcomes, no study has documented the male partners' perspective of this distressing problem and its potential influence on their psychosexual adaptation. Aim. To identify whether male partners' attributions for vestibulodynia are possible predictors of their dyadic adjustment, sexual functioning, sexual satisfaction, and psychological distress, as well as of women's pain and sexual functioning. Methods. Thirty-eight women with vestibulodynia first completed measures of pain intensity and sexual functioning. Male partners responded to mailed questionnaires assessing their own attributions for genital pain as well as their psychological distress, relationship adjustment, sexual functioning, and sexual satisfaction. Main Outcome Measures. Women completed the McGill-Melzack Pain Questionnaire (MPQ) and the Female Sexual Function Index (FSFI). Attributions of male partners were measured using an adapted version of the Attributional Style Questionnaire (ASQ)-Partner Version. Men also filled out the Brief Symptom Inventory (BSI), the Dyadic Adjustment Scale (DAS), the Sexual History Form (SHF), and the Global Measure of Sexual Satisfaction (GMSEX). Results. All four negative attribution dimensions and higher levels of women's pain intensity successfully predicted increased psychological distress in male partners. Higher levels of both internal and global attributions were associated with men's poorer dyadic adjustment, whereas global and stable attributions were related to their lower sexual satisfaction. Attributions failed to significantly predict sexual functioning in male partners and women's pain and sexual functioning. Conclusions. Evaluation and treatment of sexual pain problems should involve both partners and should explore the role of negative attributions.

Somatization and psychological distress among women with vulvar vestibulitis syndrome.

Zolnoun D, Park EM, Moore CG, Liebert CA, Tu FF, As-Sanie S
Int J Gynaecol Obstet. 2008 Jul 15. [Epub ahead of print]

OBJECTIVE: To investigate the distribution of psychological characteristics and pain reporting among women with vulvar vestibulitis syndrome (VVS). METHODS: In this exploratory study, 109 women with VVS completed a battery of questionnaires to assess pain with intercourse and psychological characteristics (e.g. somatization, anxiety, distress). The distribution of these characteristics was compared, first with a conventional binary classification schema (primary and secondary) and

subsequently with a 3-category schema (primary, latent primary, secondary). RESULTS: Severity of pain with intercourse did not differ among the subgroups using either classification schema. Women with primary VVS consistently showed higher levels of somatization, anxiety, and distress compared with those with secondary VVS. Using a 3-tiered classification system, we found no difference between latent primary diagnosis and the other 2 groups (primary and secondary). CONCLUSION: This study highlights the critical need for research on subtype definition and the role of psychological factors in VVS.

Review of the literature on the psychoemotional reality of women with vulvodynia: Difficulties met and strategies developed.

[article in French]

Cantin-Drouin M, Damant D, Turcotte D
Pain Res Manag. 2008 May-Jun;13(3):255-63.

BACKGROUND: Within the past three decades, increased attention has been placed on the study of vulvodynia -- an unexplained chronic vulvular discomfort felt without any related pathology. In addition to its physical implications, vulvodynia has a psychosocial dimension. OBJECTIVE: The purpose of the current article is to present a review of the literature on the psychoemotional reality of women with vulvodynia. METHOD: A systematic literature review was conducted in the main social sciences databases, such as Dissertation Abstracts, Current Contents and PsycINFO. RESULTS: Although some discrepancies were found in study results, the review of the literature revealed that women with vulvodynia are often confronted with identity and psychological difficulties, which are, in turn, influenced by social standards regarding sexuality and femininity. To cope with these difficulties, women develop different strategies to decrease the stress related to pain and enhance their psychological well-being. CONCLUSION: The psychological and relational difficulties experienced by women with vulvodynia are not only due to the physical pain but also to the meaning they attribute to it, often influenced by social expectations related to heterosexuality and femininity. Hence, it is important to assist these women by increasing their knowledge on the psychosocial aspects of their experience while taking into account influences from the social context.

Other Vulvovaginal Disorders

Determining the cause of vulvovaginal symptoms.

Farage MA, Miller KW, Ledger WJ
Obstet Gynecol Surv. 2008 Jul;63(7):445-64.

Both patients and clinicians may incorrectly diagnose vulvovaginitis symptoms. Patients often self-treat with over-the-counter antifungals or home remedies, although they are unable to distinguish among the possible causes of their symptoms. Telephone triage practices and time constraints on office visits may also hamper effective diagnosis. This review is a guide to distinguish potential causes of vulvovaginal symptoms. The first section describes both common and uncommon conditions associated with vulvovaginitis, including infectious vulvovaginitis, allergic contact dermatitis, systemic dermatoses, rare autoimmune diseases, and neuropathic vulvar pain syndromes. The focus is on the clinical presentation, specifically 1) the absence or presence and characteristics of vaginal discharge; 2) the nature of sensory symptoms (itch and/or pain, localized or generalized, provoked, intermittent, or chronic); and 3) the absence or presence of mucocutaneous changes, including the types of lesions observed and the affected tissue. Additionally, this review describes how such features of the clinical presentation can help identify various causes of vulvovaginitis.

Mannose-binding lectin gene polymorphism and resistance to therapy in women with recurrent vulvovaginal candidiasis.

Donders GG, Babula O, Bellen G, Linhares IM, Witkin SS
BJOG. 2008 Sep;115(10):1225-31.

PRECIS: Women with recurrent vulvovaginal candidiasis (RVC) due to a polymorphism in codon 54 of the MBL2 gene respond better to fluconazole maintenance therapy than do women with other underlying causes. **OBJECTIVE:** To explain differences in response rates to maintenance therapy with fluconazole in women suffering from RVC by evaluating associations with a polymorphism in the gene coding for mannose-binding lectin (MBL). **DESIGN:** Follow-up study, nested case-control group. **SETTING:** Women attending vulvovaginitis clinic for RVC. **POPULATION:** Women participating in a multicentric study in Belgium with a degressive dose of fluconazole for RVC (the ReCiDiF trial) were divided into good responders, intermediate responders and nonresponders according to the number of relapses they experienced during therapy. From 109 of these women with adequate follow-up data, vaginal lavage with 2 ml of saline were performed at the moment of a proven acute attack at inclusion in the study, before maintenance treatment was started. A buccal swab was obtained from 55 age-matched women without a history of Candida infections, serving as a control group. **METHODS:** Extracted DNA from buccal or vaginal cells was tested for codon 54 MBL2 gene polymorphism by polymerase chain reaction and endonuclease digestion. **MAIN OUTCOME MEASURES:** Frequency of MBL2 codon 54 allele B in women with optimal or poor response to maintenance therapy in composition with controls. Results Women (n = 109) suffering from RVC were more likely to carry the variant MBL2 codon 54 allele B than control women (20 versus 6.6%, OR 3.4 [95% CI 1.3-8.2], P = 0.01). B alleles were present in 25% of the 36 women not suffering from any recurrence during the maintenance therapy with decreasing doses of fluconazole (OR 4.9 [95% CI 1.9-12.5], P = 0.0007 versus controls), in 20% of the 43 women with sporadic recurrences (OR 3.6 [95% CI 1.4-9.2], P = 0.007 versus controls) and in 15% of the 30 women who had to interrupt the treatment regimen due to frequent relapses (P = 0.097 versus controls). **CONCLUSIONS:** The MBL2 codon 54 gene polymorphism is more frequent in Belgian women suffering from RVC than in controls. The presence of the B allele is associated with a superior response to fluconazole maintenance therapy as compared with RVC patients without this polymorphism. We conclude that RVC due to deficient MBL production is more easily helped with antifungal medication than is RVC due to some other mechanism.

Effect of antibiotics on vulvovaginal candidiasis: a MetroNet study.

Xu J, Schwartz K, Bartoces M, Monsur J, Severson RK, Sobel JD
J Am Board Fam Med. 2008 Jul-Aug;21(4):261-8.

PURPOSE: Vulvovaginal candidiasis (VVC) is believed common after systemic antibiotic therapy, yet few studies demonstrate this association. In this pilot study, we evaluate the effect of short-course oral antibiotic use on VVC. **METHODS:** Nonpregnant women aged 18 to 64 years who required ≥ 3 days oral antibiotics for nongynecological diseases were recruited from a family medicine office. Age-matched (± 5 years) women seen in the same clinic for noninfectious problems were recruited as controls. The main outcomes are incidence of symptomatic VVC and prevalence of positive vaginal Candida culture 4 to 6 weeks after antibiotics. **RESULTS:** Eighty (44 in antibiotic group) women were recruited; 14 of 79 (95% CI, 0.11-0.28) had asymptomatic vaginal Candida cultures positive at baseline. During follow-up, 10 of 27 (95% CI, 0.22-0.56) women in antibiotic group were Candida culture positive. In contrast, 3 of 27 (95% CI, 0.04-0.28) women in the control group were Candida culture positive (relative risk, 3.33; P = .03). Meanwhile, 6 of 27 (95% CI, 0.11-0.41) women in antibiotic group developed symptomatic VVC whereas none (95% CI, 0-0.12) of the women in the control group developed vaginal symptoms (relative risk, infinity; P = .02). Baseline Candida culture did not predict subsequent symptomatic VVC after antibiotics. **CONCLUSION:** In this pilot study, the use of short courses of oral antibiotics seems to increase prevalence of asymptomatic vaginal Candida colonization and incidence of symptomatic VVC. Larger cohort studies are needed to confirm these findings.

Systemic and mucosal immunization with Candida albicans hsp90 elicits hsp90-specific humoral response in vaginal mucosa which is further enhanced during experimental vaginal candidiasis.

Raska M, Belakova J, Horynova M, Krupka M, Novotny J, Sebestoya M, Weigl E
Med Mycol. 2008 Aug;46(5):411-20. Epub 2008 Mar 5

The *Candida albicans* heat shock protein 90 kDa (hsp90-CA) is an important target for protective antibodies in disseminated candidiasis of experimental mice and humans. Hsp90-CA is present in the cell wall of *Candida* pseudohyphae or hyphae--typical pathogenic morphotypes in both mucosal and systemic *Candida* infections. However, the potential protective effects of hsp90-CA-specific antibodies in vaginal candidiasis has not yet been reported. In the present study we used various vaccine formulations (recombinant hsp90-CA protein and hsp90-CA-encoding DNA vaccine) and routes of administration (intradermal, intranasal, and intravenous) to induce both hsp90-CA-specific systemic and vaginal mucosa immune responses in experimental BALB/c mice. The results showed that intradermal recombinant hsp90-CA protein priming, followed by intranasal or intradermal recombinant hsp90-CA protein boosting induced significant increases in both serum and vaginal hsp90-CA-specific IgG and IgA antibodies compared to the control group, as well as enhanced hsp90-CA-specific splenocyte responses *in vitro*. In the intradermally boosted group, subsequent experimental vaginal *Candida* infection induced additional increases in the hsp90-CA specific IgG isotype, suggesting that *Candida* has the ability to induce a local hsp90-specific antibody (IgG) response during vulvovaginal candidiasis. Further work is required to elucidate the importance of immunity to highly conserved antigens during infection of the human female reproductive tract where a balance between immunity to and tolerance for commonly antigens such as hsp90 is necessary for the maintenance of fertility.

A novel polyherbal microbicide with inhibitory effect on bacterial, fungal and viral genital pathogens.

Talwar GP, Dar SA, Rai MK, Reddy KV, Mitra D, Kulkarni SV, Doncel GF, Buck CB, Schiller JT, Muralidhar S, Bala M, Agrawal SS, Bansal K, Verma JK
Int J Antimicrob Agents. 2008 Aug;32(2):180-5. Epub 2008 Jun 20.

A polyherbal cream (Basant) has been formulated using diferuloylmethane (curcumin), purified extracts of *Embllica officinalis* (Amla), purified saponins from *Sapindus mukorossi*, Aloe vera and rose water along with pharmacopoeially approved excipients and preservatives. Basant inhibits the growth of WHO strains and clinical isolates of *Neisseria gonorrhoeae*, including those resistant to penicillin, tetracycline, nalidixic acid and ciprofloxacin. It has pronounced inhibitory action against *Candida glabrata*, *Candida albicans* and *Candida tropicalis* isolated from women with vulvovaginal candidiasis, including three isolates resistant to azole drugs and amphotericin B. Basant displayed a high virucidal action against human immunodeficiency virus HIV-1NL4.3 in CEM-GFP reporter T and P4 (Hela-CD4-LTR-betaGal) cell lines with a 50% effective concentration (EC50) of 1:20000 dilution and nearly complete (98-99%) inhibition at 1:1000 dilution. It also prevented the entry of HIV-1(IIIB) virus into P4-CCR5 cells (EC50 approximately 1:2492). Two ingredients, Aloe and Amla, inhibited the transduction of human papillomavirus type 16 (HPV-16) pseudovirus in HeLa cells at concentrations far below those that are cytotoxic and those used in the formulation. Basant was found to be totally safe according to pre-clinical toxicology carried out on rabbit vagina after application for 7 consecutive days or twice daily for 3 weeks. Basant has the potential of regressing vulvovaginal candidiasis and preventing *N. gonorrhoeae*, HIV and HPV infections.

An open trial of 5-aminolevulinic acid photodynamic therapy for vulvar lichen sclerosis.

Sotiriou E, Panagiotidou D, Ioannidis D
Eur J Obstet Gynecol Reprod Biol. 2008 Sep 6. [Epub ahead of print]

No abstract available.

The surgical management of vulvar lichen sclerosis refractory to medical management.

Rojavin Y, Salgado CJ, Hsu PW, Liu J, Aikins JK
J Plast Reconstr Aesthet Surg. 2008 Jul;61(7):848-9. Epub 2008 Apr 25.

No abstract available.

Basic Science

Pudendal motoneurons of the rat located in separated spinal nuclei possess nicotinic acetylcholine receptors having distinct pharmacological profiles.

Ogier R, Tribollet E, Bertrand D, Raggenbass M
Eur J Neurosci. 2008 Aug 8. [Epub ahead of print]

Pudendal motoneurons are located in the ventral horn of the caudal lumbar spinal cord and innervate striated pelvic muscles implicated in sexual and eliminative functions. In rats they are distributed in the dorsomedial (DM) and dorsolateral (DL) nucleus. In male rats, dorsomedial motoneurons innervate the bulbocavernosus, the levator ani and the external anal sphincter, whereas dorsolateral motoneurons control the ischiocavernosus and external urethral sphincter. Using spinal cord slices of young male rats and whole-cell patch-clamp recordings, we investigated the sensitivity of pudendal motoneurons to nicotinic cholinergic agonists. Motoneurons were identified following 1,1'-dilinoleyl-3,3',3'-tetramethylindocarbocyanine, 4-chlorobenzenesulphonate retrograde labelling. In the presence of atropine, both dorsomedial and dorsolateral motoneurons responded to acetylcholine (ACh) by generating a rapidly activating inward current. By using selective nicotinic antagonists and a nicotinic positive allosteric modulator, we found that nicotinic ACh receptors present in dorsomedial and dorsolateral motoneurons display distinct pharmacological profiles. Whereas the former are of the heteromeric type, the latter are predominantly of the alpha7-containing type. These data were confirmed by light microscopic autoradiography. In young rats, a ligand for heteromeric nicotinic receptors labelled all laminae of the central grey matter, whereas in the ventral part of the central grey, a ligand selective for alpha7-containing nicotinic receptors labelled the DL but not the DM. Dorsolateral and dorsomedial motoneurons innervate two distinct groups of pelvic muscles. A difference in their nicotinic pharmacology may be clinically relevant, as it might allow a selective pharmacological intervention in view of influencing the activity of one or the other set of muscles.

Activation of somatosensory afferents elicit changes in vaginal blood flow and the urethrogenital reflex via autonomic efferents.

Cai RS, Alexander MS, Marson L
J Urol. 2008 Sep;180(3):1167-72. Epub 2008 Jul 18.

PURPOSE: We examined the effects of pudendal sensory nerve stimulation and urethral distention on vaginal blood flow and the urethrogenital reflex, and the relationship between somatic and autonomic pathways regulating sexual responses. **MATERIALS AND METHODS:** Distention of the urethra and stimulation of the pudendal sensory nerve were used to evoke changes in vaginal blood flow (laser Doppler perfusion monitoring) and pudendal motor nerve activity in anesthetized, spinally transected female rats. Bilateral cuts of either the pelvic or hypogastric nerve or both autonomic nerves were made, and blood flow and pudendal nerve responses were reexamined. **RESULTS:** Stimulation of the pudendal sensory nerve or urethral distention elicited consistent increases in vaginal blood flow and rhythmic firing of the pudendal motor nerve. Bilateral cuts of the pelvic plus hypogastric nerves significantly reduced vaginal blood flow responses without altering pudendal motor nerve responses. Pelvic nerve cuts also significantly reduced vaginal blood flow responses. In contrast, hypogastric nerve cuts did not significantly change vaginal blood flow. Bilateral cuts of the pudendal sensory nerve blocked pudendal motor nerve responses but stimulation of the central end evoked vaginal blood flow and pudendal motor nerve responses. **CONCLUSIONS:** Stimulation of the sensory branch of the pudendal nerve elicits vasodilatation of the vagina. The likely mechanism is via activation of spinal pathways that in turn activate pelvic nerve efferents to produced changes in vaginal blood flow. Climatic-like responses (firing of the pudendal motor nerve) occur in response to stimulation of the pudendal sensory nerve and do not require intact pelvic or hypogastric nerves.

TRPV1 mediates the uterine capsaicin-induced NMDA NR2B-dependent cross-organ reflex sensitization in anesthetized rats.

Peng HY, Chang HM, Chang SY, Tung KC, Lee SD, Chou D, Lai CY, Chiu CH, Chen GD, Lin TB
Am J Physiol Renal Physiol. 2008 Jul 16. [Epub ahead of print]

Spinal cord-mediated cross-organ sensitization between the uterus and the lower urinary tract may underlie the high concurrence of obstetrical/gynecological inflammation and chronic pelvic pain syndrome characterized by urogenital pain. However, the neural pathway and the neurotransmitters involved are still unknown. We tested the hypothesis that the excitation of capsaicin-sensitive primary afferent fibers arising from the uterus through the stimulation of transient receptor potential vanilloid 1 (TRPV1), induces cross-organ sensitization on the pelvic-urethra reflex activity. Capsaicin (1-1000 μ M, 0.05 cc) was instilled into the uterus to induce cross-organ reflex sensitization. Activation of capsaicin-sensitive primary afferent fibers by capsaicin instillation into the uterine horn sensitized the pelvic-urethra reflex activity that was reversed by an intra-uterine pretreatment with capsaizepine, a TRPV1-selective antagonist. Intrathecal injection of AP5, a glutamatergic N-methyl-D-aspartate (NMDA) antagonist, and Co-101244, an NMDA NR2B-selective antagonist, both abolished the cross-organ reflex sensitization caused by capsaicin instillation. These results demonstrated that TRPV1 plays a crucial role in contributing to the capsaicin-sensitive primary afferent fibers mediating the glutamatergic NMDA-dependent cross-organ sensitization between the uterus and the lower urinary tract when there is a tissue injury.

Clitoral sexual arousal: Neuronal tracing study from the clitoris through the spinal tracts.

Martin-Alguacil N, Schober JM, Sengelaub DR, Pfaff DW, Shelley DN
J Urol. 2008 Aug 14. [Epub ahead of print]

PURPOSE: Although genital tactile stimulation is regarded as a precursor to sexual arousal and a recognized initiator of central nervous system arousal, specific afferent neural pathways transmit sensory stimuli of arousal, beginning at the epithelial level on the clitoris and following the course of arousal stimuli through the central nervous system. Limited knowledge exists of the pathway from the cutaneous receptors of nerves originating in the epithelial tissue of the clitoris and continuing to spinal cord afferents. Such information may contribute to an understanding of sexual arousal, particularly in female vertebrates. We further defined the neural pathways and mechanisms responsible for arousal originating in the epithelium of the clitoris as well as related neural pathways to the spinal cord in a murine model. **MATERIALS AND METHODS:** We performed a comprehensive review of the published relevant clinical and histological material from human and nonhuman vertebrate studies. In 29 adult female C57B1/6 mice the distribution of pelvic nerves and vessels was mapped. Gross dissection of 4 female mice was facilitated by resin injection of the vascular system in 2. Neuronal tracing was performed in 25 mice that received clitoral injection of wheat germ agglutinin-horseradish peroxidase into the clitoris and were sacrificed after 72 to 96 hours. The spinal cord and periclitoral tissue were removed and fixed. Immunohistochemistry was performed. **RESULTS:** Gross anatomy of the mouse clitoris showed that pudendal and hypogastric nerves have a major role in the innervation of the external genitalia. Neuronal tracing revealed that the greatest nerve density was noted in the L5/6 spinal cord. The distribution extended from S1 to L2 with no labeling seen in the L3 spinal cord. Wheat germ agglutinin-horseradish peroxidase labeling was seen caudal in levels S1 through L4 and rostral in L2. **CONCLUSIONS:** Understanding the neuroanatomy of the clitoris using a murine model may provide a valuable tool for the study of sexual arousal disorders and the further understanding of sexual function related to neural pathologies and trauma.